PB80-211428

Amitraz (BAAM)
Position Document 4

(U.S.) Environmental Protection Agency
Arlington, VA

4 Jun 79

U.S. Department of Commerce
National Technical Information Service
NTIS

50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO. EPA/SPRD-80/25	2.	PB80-211428
4. Title and Subtitle: Amitraz (BAAM): Position Document 4			5. Report Date: 6/4/79 6.
7. Author(s)			8. Performing Organization Rept. No.
9. Performing Organization Name and Address: Special Pesticide Review Division Environmental Protection Agency Crystal Mall #2 Arlington, VA			10. Project/Task/Work Unit No. 11. Contract(C) or Grant(G) No. (C) (G)
12. Sponsoring Organization Name and Address: Environmental Protection Agency 401 M St. S.W. Washington, D.C. 20460			13. Type of Report & Period Covered 14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

Agency Regulatory Decision on Registration of Pesticide: Also contains comments from USDA and Scientific Advisory Panel and EPA's response to these concerns on economic, agricultural, environmental and health impact of the regulatory decision.

17. Document Analysis a. Descriptors

0504,0606,0703

b. Identifiers/Open-Ended Terms

0606

c. COSATI Field/Group

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

18. Availability Statement: Release Unlimited	19. Security Class (This Report): Unclassified	21. No. of Pages
	20. Security Class (This Page): Unclassified	22. Price

EPA/SPRD-80/25

AMITRAZ (BAAM): POSITION DOCUMENT 4

SPECIAL PESTICIDE REVIEW DIVISION
OFFICE OF PESTICIDE PROGRAMS
OFFICE OF TOXIC SUBSTANCES
U.S. ENVIRONMENTAL PROTECTION AGENCY

JUN 4 1979

ACKNOWLEDGEMENTS

Writing Staff
Jeff Kempter, Project Manager, SPRD, OPP
Paul N. Parsons, Writer-Editor, SPRD, OPP

EPA Project Support Team
Fred Arnold, Regulatory Analyst, SPRD, OPP
Merry Lou Alexander, Aquatic Biologist, HED, OPP
Laura Bennett, Physiologist, HED, OPP
Dr. George Beusch, Chemist, HED, OPP
Richard Bozof, Attorney, OGC
Edwin Budd, Toxicologist, HED, OPP
Carolyn Gregorio, Toxicologist, HED, OPP
Dr. C. Hiremath, Toxicologist, CAG
Phillip O. Hutton, Entomologist, RD, OPP
Mark Luttner, Economist, BFSD, OPP
Dr. Robert McGaughy, Toxicologist, CAG
Abraham Mittelman, Chemist, HED, OPP
William S. Rabert, Aquatic Biologist, HED, OPP
Dr. David Severn, Chemist, HED, OPP
Robert Stapp, Entomologist, BFSD, OPP
Geraldine Werdig, Branch Chief, SPRD, OPP

EPA Pesticide Chemical Review Committee (PCRC)
Dr. William A. Wells, Chairperson, SPRD, OPP
Dr. Elizabeth Anderson, CAG, ORD
Dr. Richard N. Hill, OTS
Dr. Allen Jennings, SRD, OPM
Dr. Donna Kuroda, OHEE, ORD
Mr. John J. Neylan, PED, OE
Mr. Michael S. Winer, OGC

TABLE OF CONTENTS

Page

I. Introduction.....1

II. Analysis of Comments.....5

A. Comments Relating to Risk

1. Lymphoreticular Tumors in Female CFLP Mice.....6

2. Oncogenicity of a Metabolite: 2,4-dimethylaniline..... 9

3. Mutagenicity of 2,4-dimethylaniline.....12

4. Overall Evaluation of the Oncogenicity of Amitraz.....14

5. Risk Assessment.....15

B. Comments Relating to Benefits

1. Pears.....17

2. Apples.....17

C. Comments Relating to Regulatory Options

1. Pears - Conditional Registration and Restricted Use.....21

2. Apples - Denial of Registration.....27

III. Conclusions.....32

Bibliography

Appendix A - List of Comments

Appendix B - SAP and USDA Comments

AMITRAZ (BAAM): POSITION DOCUMENT 4

I. Introduction

Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended (FIFRA) (7 U.S.C. Section 136 et. seq.), the Environmental Protection Agency (EPA or the Agency) regulates all pesticide products. On June 22, 1976, the Upjohn Company applied to the Agency for registration of amitraz (BAAM EC), a chemical which had not been previously registered for use in the United States.

Section 3(c)(5) of FIFRA sets forth the conditions for approval of a registration. It directs the Administrator to register a pesticide if:

(A) its composition is such as to warrant the proposed claims for it;

(B) its labeling and other material required to be submitted comply with the requirements of (FIFRA);

(C) it will perform its intended function without unreasonable adverse effects on the environment, and

(D) when used in accordance with commonly recognized practice it will not generally cause unreasonable adverse effects on the environment.[1]

Section 3(c)(6) states that if the requirements of 3(c)(5) are not satisfied, the Administrator may deny the registration application. The Agency must notify the applicant of his decision and his reasons for doing so, and publish a notice in the Federal Register allowing the applicant 30 days to respond. The applicant may either correct any conditions specified by the Administrator, or seek relief by requesting a hearing via the processes described in Section 6 of FIFRA.

Section 3(c)(7)(C) of FIFRA allows the Administrator to conditionally register a new pesticide containing an unregistered active ingredient under special circumstances, even though all the data requirements for full registration have not been met. Specifically, the Administrator may conditionally register such a pesticide for a period reasonably sufficient for the generation and submission of required data if:

---

[1] "Unreasonable adverse effects" is defined by Section 2(bb) of FIFRA as "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."

— the required data are lacking because a period reasonably sufficient for the generation of the data has not elapsed since the Administrator first imposed the data requirement,

— by the end of the conditional registration the submitted data do not meet or exceed the risk criteria listed in the Agency's regulations (40 CFR 162.11),

— the use of the pesticide during such period will not cause any unreasonable adverse effect on the environment, and

— the use of the pesticide is in the public interest.

On March 30, 1977, the Agency determined that the use of amitraz may result in unreasonable adverse effects and issued a Rebuttable Presumption Against Registration (RPAR). The Agency designed the Rebuttable Presumption Against Registration (RPAR) process to gather risk and benefit information about pesticides suspected of posing certain adverse effects and to make balanced decisions concerning them in a manner which allows all interested groups to participate. This process is set forth in 40 CFR 162.11. A Federal Register notice on April 6, 1977 announced the availability of Position Document 1 to support the RPAR (42 FR 18299-18302).

After reviewing rebuttal comments received in response to Position Document 1, the Agency issued a notice of determination and availability of Position Document 3 in the Federal Register on January 12, 1979 (44 FR 2678-2682). In Position Document 3 the Agency analyzed the rebuttals, presented its analysis of the risks and benefits from the uses of amitraz, and proposed a decision to conclude the RPAR process. The decision was to conditionally register amitraz for 4 years on pears, during which more risk and benefit data would be generated, and to deny the registration of amitraz on apples.

When issuing a notice of intent to cancel or intent to hold a hearing under Section 6(b) of FIFRA, the Administrator must submit such notices to the Secretary of Agriculture and to the Scientific Advisory Panel for their review and comment. Because the decisions described in this notice were made with respect to the registration and conditional registration provisions of Section 3, the Agency is not required to submit notice of these decisions to the Secretary of Agriculture or to the SAP. However, the Agency in its discretion has elected to follow the procedure for notices issued under Section 6. In addition, the Agency has afforded registrants and other interested persons an opportunity to comment on the decision described in Position Document 3 and the January 12, 1979 Notice of Determination.

The Agency received and considered three timely sets of comments in response to the January 12, 1979 Notice of Determination and the Amitraz Position Document 3. The Agency also considered four comments which were received after the mandatory 30-day period allowed by law. All comments received either during or after the 30-day period were made available in the public file for review and evaluation by the public. Responses from the SAP, the U.S. Department of Agriculture, and other interested parties have been analyzed and are addressed in Section II of this document. Section III summarizes the Agency's decision concerning pesticide products containing amitraz. Appendix A lists all comments received by the Agency. Appendix B contains the responses from the SAP and the USDA in their entirety.

II. Analysis of Comments

The Agency received comments from the Secretary of Agriculture, the Scientific Advisory Panel (SAP), and five other concerned individuals and organizations. These comments are organized by topic and discussed in this section. The Agency has changed some aspects of its risk assessment, benefits, and regulatory options in response to the comments. Except as discussed, the Agency has not changed any other aspects of its analysis in Position Document 3.

A. Comments Relating to Risk

1. Lymphoreticular (LR) Tumors in Female CFLP Mice

The amitraz risk assessment was based primarily on a mouse oncogenic bioassay by the Boots Chemical Company (Burnett et al., 1976). This Boots study, according to its authors and several EPA pathologists, showed a statistically significant increase in lymphoreticular (LR) tumors in female mice ingesting amitraz. Position Document 3 outlined the key issues and the opinions of several pathologists on the protocols and results of that study.

One commenter [2A(30000/12B)] submitted two additional pathologists' opinions on the histopathological results of the Boots mouse study. These pathologists, Dr. Maurice C. Lancaster of the Boots Company and Dr. Thomas J. Kakuk of the Upjohn Company, independently examined the lymphoid tissues of the female mice, apparently without knowledge of the dose group for the animals (i.e., so that they read the slides "blind," or without bias). They each concluded that there was not a statistically significant incidence of LR tumors in the high-dose females compared to the controls. Using these opinions, the commenter stated, "[I]t can be concluded that amitraz (BTS-27419) should not be regarded as a weak carcinogen nor should amitraz accordingly present any human health risk for the uses specified."

Commenter 2A(30000/12B) also testified before the Scientific Advisory Panel on January 25, 1979, and requested the Agency to consider his testimony [comments 2C and 2D (30000/12)] as part of his comments. At the SAP meeting, Dr. Kakuk [comment 2D(30000/12B)] explained his findings and those of Dr. Lancaster. He asserted that the difference between their pathology diagnoses and those of the other pathologists "was due to the recognition or the lack thereof of microscopically detectable LR tumors...and the failure to differentiate them from reactive inflammatory lesions (hyperplasia, lymphadenitis, etc.)." He also stated that the original three Boots Study pathologists and Dr. Reuber (for EPA) had "overdiagnosed the frequency of LR tumors." While not refuting the positive findings of Dr. Dubin (after consultation with Dr. Squire), Dr. Kakuk concluded that the incidence of LR tumors in the high-dose female mice was not significantly greater than the LR tumor incidence in the matched controls.

The Agency's Carcinogen Assessment Group reviewed these most recent reports of Drs. Lancaster and Kakuk (Albert 1979). The CAG indicated that these reports did not change the CAG's previous position that "the evidence is weakly positive that amitraz is likely to be a human carcinogen." Dr. Kakuk's report had restated the main pathology issue which the Agency has faced throughout the RPAR review of

amitraz: namely, how to definitively distinguish microscopic lymphoreticular tumors from precursor lesions and from reactive inflammatory hyperplasia. As explained by Dr. Dubin in his diagnosis (Albert 1979), an LR tumor develops along a continuous progression from preneoplastic hyperplasia to a fully malignant lymphoma. Because of the lack of uniformly accepted criteria, some pathologists might identify a specific lesion as hyperplasia, while others would call it a lymphoma. Dr. Dubin has also pointed out the potential for confusing LR tumors with slight chronic inflammation of tissue. Given the lack of agreed-upon criteria for positively identifying LR tumors, the Agency expects differences among the diagnoses of reputable pathologists, and differences were indeed seen in this case. The Agency finds that the additional comments and diagnoses by Drs. Kakuk and Lancaster did not resolve the issue and did not negate the opinions of the original Boots pathologists, of Dr. Reuber or of Drs. Dubin and Squire jointly, who found a statistically significant lymphoreticular tumor response in the high dose female mice.

The Scientific Advisory Panel [Comment 3(30000/12B)] reviewed the Boots mouse study and the diagnoses of the study's three pathologists, of Dr. Reuber, of Dr. Dubin, of Drs. Dubin and Squire jointly, of Dr. Lancaster and of Dr. Kakuk. The SAP concluded, "From consideration of all these

data, the Panel is of the opinion that a statistically significant increase in mouse lymphoma has not been shown." The SAP also recommended that a new mouse oncogenicity study be performed. The SAP did not explain its reasons for reaching these conclusions.

In response to the SAP's conclusion that a statistically significant increase in mouse lymphoma has not been demonstrated, the Agency replies that the absence of carcinogenic effect has by no means been demonstrated, since two reputable pathologists in addition to the original Boots pathologists concluded that lymphoreticular tumors were induced by amitraz. Further, the SAP has not provided any reason for rejecting the diagnoses of these pathologists. Therefore, the Agency concludes that the Boots mouse study provides weakly positive evidence that amitraz is a possible human carcinogen. The Agency agrees with the SAP that a new mouse oncogenicity study be carried out, because of the deficiencies of that experiment which were described in Position Document 3.

2. Oncogenicity of a Metabolite: 2,4-dimethylaniline

Commenters 2A(30000/12B) and 2D(30000/12B) contested the Agency's conclusion that 2,4-dimethylaniline may present an oncogenic risk to man. The commenters agreed that an NCI

study has shown a statistically significant difference between the incidence of pulmonary tumors (11/19) in female mice treated at the high dose and the incidence of those tumors (5/22) in the matched control females ($p<.025$). However, the commenters asserted that this evidence does not justify labeling the compound a carcinogen, because:

(1) 34% of the pooled control female mice had not been pathologically examined.

(2) There were more sarcomas and malignant tumors in the matched control female mice than in treated female mice.

(3) The Boots mouse study with amitraz did not show an increase of pulmonary tumors.

(4) 2,4-dimethylaniline did not induce LR tumors in the NCI study.

(5) The author of the NCI study on 2,4-dimethylaniline stated that since only one sex of one species was affected at one site, "such findings are contrary to the criteria of the NCI Subcommittee on Environmental Carcinogenesis, in which greater

confidence is placed on a dose-dependent relationship and positive results in more than one group of animals."

Point (1) refers to the "pool" of six control groups that were run during the NCI's 9 month study of 21 compounds. However, when comparing treated groups to control groups to determine the statistical significance of tumor incidences, it is appropriate to compare the treated group to its matched control group. This was the procedure followed in the NCI study. The fact that 100% of the matched controls and the treated animals were examined should dispel any question of irregularity concerning the protocol.

In point (2), the commenters combined the incidences of tumors at several sites and compared these combined incidences to the matched control animals. This approach is not as definitive as evaluating the tumor incidence for specific sites. In addition, in order to demonstrate that a chemical is not an oncogen, a bioassay may not show positive tumorigenic activity at any site. Thus, the Agency does not recognize the commenter's point as meaningful.

Point (3) does not negate the NCI study's finding that 2,4-dimethylaniline induced pulmonary tumors. Since different strains were used in the Boots and NCI studies, the results

are not comparable. Further, the Boots study may not have been sensitive enough to detect on oncogenic response caused by this metabolite.

Point (4) is factually correct but is irrelevant to the potential carcinogenicity of 2,4-dimethylaniline, which is based on its induction of pulmonary tumors in the NCI study.

Regarding point (5), the Agency's conclusion that 2,4-dimethylaniline is a potential human carcinogen is based upon the statistically significant higher incidence of lung tumors in high dose female mice compared to the matched controls. Although a significant finding in more than one dose group and a positive dose-response relationship would indicate a stronger effect, the positive finding in one group is sufficient evidence of a presumptive cancer risk.

3. Mutagenicity of 2,4-dimethylaniline

Commenter 2D (30000/12B) asserted that Position Document 3 was "somewhat misleading" in that it described the one positive response obtained for 2,4-dimethylaniline in the TA100 strain of the Ames test, but did not mention the negative results for other tests on that chemical, on amitraz, or on other metabolites of amitraz.

The Agency refers the commenter to page 18, paragraph 4, of Position Document 3, which states:

> The CAG also reviewed mutagenic test data submitted by the registrant [on 2,4-dimethylaniline] and found a positive mutagenic response in one strain (TA 100) of bacteria (S. typhimurium). The data in three replicate dose-response curves appeared to be accurate and valid (Albert 1978a). No mutagenic response was seen in the other four [Ames Test] strains of bacteria tested [for 2,4-dimethylaniline]. (emphasis added)

With respect to the mutagenic test results on amitraz and metabolites other than 2,4-dimethylaniline, the Agency refers to page 18, second paragraph, of Position Document 3, which states:

> While the registrant submitted the results of several mutagenicity tests, the CAG found the data insufficient for defining amitraz as a mutagen or non-mutagen, because of deficiencies in the protocols (Albert 1978e). The authors of those tests had reported that amitraz caused no response in those tests. (emphasis added)

The Agency concluded in Position Document 3 that the single positive mutagenic result for 2,4-dimethylaniline,

together with the induction of pulmonary tumors in the NCI bioassay by this chemical, are additional evidence that amitraz may pose a carcinogenic risk.

In sum, the Agency was not misleading in its discussion and use of the mutagenic test data for amitraz and its metabolites.

4. Overall Evaluation of the Oncogenicity of Amitraz

In Position Document 3 (pp. 15-19) the Agency evaluated the overall weight of evidence concerning the oncogenicity of amitraz. The data reviewed included the Boots rat and mouse bioassays on amitraz, the NCI rat and mouse bioassays on the metabolite 2,4-dimethylaniline, and Boots-Upjohn's mutagenic studies on amitraz and several metabolites. In response to Position Document 3, the Boots and Upjohn companies jointly submitted comments rejecting the Agency's findings with respect to these studies. The Scientific Advisory Panel, however, only commented upon the issue of lymphoreticular tumors in the Boots mouse study and reached its conclusions without addressing the NCI study on 2,4-dimethylaniline or the mutagenicity data. Nevertheless, the Agency has re-

viewed all the comments and data relevant to the oncogenicity of amitraz and concludes that the positive responses observed for amitraz and 2,4-dimethylaniline constitute weakly positive evidence that amitraz is a potential human carcinogen.

5. Risk Assessment

Commenter 2C(30000/128) was concerned that the Agency has assumed that the potential oncogenic activity of amitraz is "real and definite" and that the Agency used "the most extreme pathological evaluation" for calculating risk. This commenter asserted,

> It is particularly unfair, we believe, that the recently published Notice of Determination gives no indication of the disparity in the several pathology evaluations, nor that the numerical risks cited are based on the most extreme opinion. To issue such a biased document to the public, and ask for comments, makes a mockery of a process which the Agency claims allows an open, balanced decision.

The Agency believes that Position Document 3, to which the Notice of Determination referred to as the Statement of Reasons, objectively and explicitly explained all facts, assumptions and steps used in estimating the risks associated with amitraz (see pp. 26-30, Position Document 3). In Position Document 3 the Agency was careful to caution, "the

risk estimates are neither scientific certainties nor absolute upper limits, but are used by the Agency only as rough approximations of potential health risks." Contrary to the commenter's implication, the Position Document 3 discussed the results of all pathologists' reviews of the slides (pp. 16-17, Position Document 3) and noted that the risk estimates, in order to obtain an upper-bound estimate, were based upon Dr. Reuber's analysis. Further, footnote 3 of Table 4, entitled "Potential Risks Through Dietary and Occupational Exposure to Amitraz" (p.29, PD3), made it distinctly clear that the risk numbers were founded on Dr. Reuber's count of the LR tumor incidences. Thus, it is apparent that the commenter has disregarded the discussion and explanations in Position Document 3, and that the Agency presented its risk calculations and estimates openly and objectively.

B. Comments Relating to Benefits

The Agency presented its analysis of the benefits of amitraz on pears and apples on pp. 31-49 of Position Document 3. During the rebuttal period, comments and information were invited on the economic, social and environmental benefits of the pesticide, and this information was reviewed and considered in the development of Position Document 3.

The USDA worked with the EPA to produce a Pesticide Impact Assessment (USDA, 1978), which provided the basis for the benefits analysis in Position Document 3.

1. Pears

No commenters objected to the Agency's assessment of the benefits of amitraz on pears.

2. Apples

Several parties submitted statements and additional data on the use of amitraz on apples.

Commenter 2B(30000/12B) provided a large volume of efficacy and benefits data for amitraz on apples. The commenter asserted that the need for new apple miticides is "very real," but cautioned that this need is not as well documented as the need for psyllicides on pears. In support of this position, the commenter made these points:

1. The use of amitraz on apples would be limited to the North Central and Eastern States, primarily for control of European red mites.

2. Amitraz would provide growers in these states an alternative miticide where they are having difficulty obtaining control with current miticides.

3. Amitraz would enable growers to reduce the development of mite resistance to current miticides.

4. Amitraz would be used in orchards where IPM programs have failed.

5. Amitraz would be used in IPM programs involving predator insects to which amitraz is not toxic.

6. Amitraz applications may be timed to mitigate the adverse effect on predator mites, such as during the early season (pink or petal fall).

7. Amitraz could be applied late in the season as a "clean-up" spray to prevent mites from depositing over-wintering eggs in the calyx of the fruit.

8. In normal spray programs (petal fall and five cover sprays), amitraz has controlled white apple leafhopper and suppressed codling moth, leaf rollers, oriental fruit moth, San Jose scale and tentiform leaf miner; the results of these programs "suggest the possibility of reducing usage of other pesticides when amitraz is used for mite control."

9. The USDA/EPA Benefits Analysis overemphasizes the per-acre cost of amitraz versus alternative

miticides; these figures "can change drastically as it is anticipated that as production of [amitraz] increases, as well as other developments, the price of [amitraz] may be considerably lower."

The Agency agrees with points 1, 2, 3, 4 and 5 made by the commenter, since these statements reiterated the findings of the USDA/EPA Benefits Analysis. That analysis had concluded that up to 52,000 acres of apples in the Eastern and North Central states would have been treated if amitraz had been available in 1978. The analysis had indicated that amitraz would likely be applied in rotation with other miticides to minimize the development of mite resistance in areas where growers were experiencing difficulty in controlling mites with current miticides. However, because several efficacious alternatives to amitraz exist the Agency considers these benefits to be speculative and insubstantial.

Further, the Agency believes that the other points made by the commenter are speculative and do not firmly establish any "real" benefits over and above those offered by currently registered miticides. Specifically, point (6) does not establish a benefit, since the commenter indicated that amitraz is "hard on predatory mites" and acknowledged that several of the alternatives are "less harmful to predator mites" or "not highly toxic to predator mites."

On point (7), the Agency appreciates the needs of food processors for clean fruit. However, as indicated by the commenter's table on alternatives, some of the current miticides already have the capability to kill adult mites and thereby prevent egg-laying in the calyx of fruit at the end of the season.

Point (8) suggests the potential for reduced use of insecticides due to the suppressive activity of amitraz against certain insects. However, the Agency is of the opinion that while amitraz is possibly sufficient for light infestations of certain insect species, it will not preclude the necessity for insecticides against stronger attacks (Hutton 1979). The Agency also notes that amitraz has limited activity against codling moth and other lepidopterous pests, and very little or no activity against apple maggot and plum curculio. Further, only certain pest complex situations will reap the benefit of additional insect suppression, and the extent to which such situations may occur is not known.

Finally, regarding point (9), the Agency recognizes that the cost of amitraz could change as production increases in the United States. However, since the magnitude and direction of a price change cannot reliably be predicted, the Agency must rely on the present price in comparing the per-acre costs of this chemical to other miticides.

The USDA [#4(30000/12B)] urged that the Agency further explore the potential benefits of amitraz on apples by granting Experimental Use Permits under Section 5 of FIFRA. The reasons for their recommendations are listed in point #1 in the Secretary of Agriculture's letter in Appendix A.

The Agency's general response to the comments on benefits is that while amitraz is an efficacious miticide, there are other currently registered miticides which are also efficacious and cheaper. The Agency will continue to consider granting further experimental use permits, special local need registrations or emergency exemptions on apples or other crops on a case-by-case basis.

C. Comments Relating to Regulatory Options

1. Pears--Conditional Registration and Restricted Use.

In Position Document 3, the Agency proposed to conditionally register amitraz for use on pears for 4 years. The conditions of registration were that the applicant for registration would have to repeat an oncogenic bioassay of amitraz in female mice, to submit additional benefits data, and to report annually on progress and test results. In Position Document 3 the Agency also proposed to initially

classify amitraz for restricted use on pears and to modify the label to include these use instructions:

Restricted Use Pesticide. For retail sale to and use only by certified applicators or persons under their direct supervision and only for those uses covered by the certified applicator's certification.

General Precautions

A. Avoid getting in eyes, on skin or on clothing.

B. Avoid breathing vapors or spray mist.

C. In case of contact with skin, wash as soon as possible with soap and plenty of water.

D. If amitraz gets on clothing, remove contaminated clothing and wash affected parts of body with soap and water. If the extent of contamination is unknown, bathe entire body thoroughly. Change to clean clothing.

E. Wash hands with soap and water each time before eating, drinking, or smoking.

F. At the end of the work day, bathe entire body with soap and plenty of water.

G. Wear clean clothes each day and launder before reusing.

Required Clothing and Equipment for mixing, loading and cleanup procedures

1. Long-sleeve shirt (fine weave)
2. Long pants (fine weave)
3. Rubber gloves
4. Apron
5. Boots

Required clothing for ground spray application:

1. Long-sleeve shirt (fine weave)
2. Long pants (fine weave)
3. Rubber gloves
4. Boots

Reentry Interval. Reentry into treated areas is prohibited until the leaves are completely dry, and in any event, until at least 24 hours after application.

Preharvest Interval. Harvest of treated pears is prohibited until 7 days after application of amitraz.

The SAP and the USDA agreed with the Agency's proposal to conditionally register amitraz for use on pears for

4 years with a 24 hour reentry period and a 7 day preharvest interval. However, while the SAP was in favor of limiting use to certified applicators wearing protective clothing, the USDA opposed this. Specifically, the USDA objected to the classification of amitraz as a restricted use pesticide, and to the protective clothing requirements. The USDA argued against restricted use, since the people applying pesticides to commercial fruit trees are knowledgeable in the handling of pesticides and since the proposed precautionary labeling would give them adequate protection. The USDA further asserted, "the 'Restricted Use' category should be limited to pesticides that, when used as directed, pose a substantial risk to the user and/or the environment." About the protective clothing requirements, the USDA stated that aprons are impractical and a cause of accidents around farm equipment, and that simultaneously requiring gloves and washing the hands before eating, drinking or smoking seemed unnecessary.

The Agency believes that, because there is a risk of cancer for applicators, amitraz must be classified for restricted use. During application of this chemical, the additional risk of cancer to the individual ranges from one in ten thousand for groundspray equipment, to three in one million for aerial application. While these numbers may

not appear significant, they are based upon an oncogenic study which must be repeated due to uncertainties in the protocols and results. The outcome of the repeat study could indicate a greater risk than is reflected by the present Boots mouse study. It is important that the Agency take precautions to reduce exposure to the maximum extent possible. Therefore, the Agency believes that only certified applicators should apply amitraz. Further, the applicators for the commercial pear orchards are likely to be already certified and experienced with the use of amitraz under the Agency's emergency use permits during 1977 and 1978.

The Agency accepts the USDA's suggestions to delete the requirements for an apron, since the apron might cause accidents. However, the Agency rejects the USDA's request to delete the requirement to wear gloves and to wash one's hands before eating, drinking or smoking, since oral exposure to amitraz should be avoided.

While agreeing with the SAP's recommendations that another mouse study be conducted, that amitraz should be conditionally registered for 4 years, and that use restrictions should be imposed, commenter 2(30000/12B) did not concur with the Agency's requirement for submission of additional benefits data. The commenter preferred that the applicant for registration be allowed to determine whether

to gather more benefits data for pears. The only reason given for this proposition opinion was that the Agency's requirement "is not reasonable."

The Agency stated clearly in Position Document 3 and still concludes that the data base used by the USDA Assessment Team for estimating the economic benefits of amitraz on pears was very weak, and that the Assessment Team's estimate was unreliable. Because the evidence suggests that amitraz poses a carcinogenic risk, the Agency anticipates that it will need empirical benefits data in order to determine whether full registration of amitraz for pears will result in any unreasonable adverse effects. Therefore, the Agency's stipulation that the applicant for registration submit additional benefits data on pears within 4 years of the date of conditional registration is a reasonable one. Neither the SAP nor the USDA objected to this data requirement.

The additional benefits data which will be required as part of the conditional registration for pears need to be specified. By "additional" data, the Agency means data in addition to that cited by the USDA Assessment Team which would support a more reliable estimate of economic benefits. Such data should include:

(1) Actual cost of amitraz versus non-amitraz spray schedules.

(2) Tree loss in plots treated with amitraz versus control plots.

(3) Percent and gross pack-out for the different grades of pears from plots treated with amitraz versus control plots.

(4) Any other relevant economic data.

2. Apples

Position Document 3 proposed that the Agency deny the application for registration of amitraz on apples, since it was concluded that the risks outweighed the benefits for that use.

Both the SAP and USDA disagreed with the Agency's consideration of risks and benefits. About the potential cancer risks, the SAP stated, "the issue of oncogenicity of BAAM is sufficiently questionable that the restriction of the use of BAAM on apples is not warranted." USDA emphasized the potential benefits of amitraz's use on apples and the "promising results" obtained in the U.S. for amitraz on several crops and domestic animals. The Secretary of Agriculture recommended that all pending experimental use

permits and applications for registration s ɔuld be re-evaluated "on their own merits." The Secre ary's statement, although not clear, apparently advocates co: litional registration of amitraz on apples.

Commenter 2C(30000/12B) was also criti: l of the Agency's position:

> We believe, frankly, that the rea: ɔns cited for denying availability of BAAM for use o: apples even during the time required to repeat the :tudy, are spurious and the conclusion therefore u warranted. First, to claim a 'negative economic ir ɔact' which assumes that growers would use a produc : which did nothing more than less expensive produc :s, and thus increase costs, is unrealistic. Secon: to state that denial would eliminate a hypothetical r .sk of the infinitesimal magnitude estimated on th : basis of the extreme 'worst case' assumptions cited, is meaningless. And then, to claim as a factor favorin: denial that such action would result in continued u :e of other available products on which comparable :tudies have not yet been carried out, is scientifically unreasonable and socially irresponsible. We suggest that a more reasonable course would be to grant con :itional registration for use on apples and thus more definitely evaluate the benefits which we believe :an be demonstrated. I remind you again that amitr .z products are registered for use on apples in various countries around the world, where benefits are re ognized.

> Finally, we are also concerned for the development of further uses of amitraz under the proposed conditions. Our currently pending applications for Experimental Use Permits for use on cotton and citrus demonstrate potentially significant usefulness, while resulting in extremely low consumer dietary exposure. Such developmental programs should not arbitrarily be held up on the basis of the data and assumptions now being discussed. (emphasis in original)

The Agency stands by its conclusion that it cannot grant either full registration or conditional registration of amitraz for use on apples. The Agency concludes that the Boots mouse study does not satisfy the Agency's data requirements for full registration under Section 3(c)(5) of FIFRA. As noted in Position Document 3, the deficiencies of the Boots study and the uncertainty of its results make this study an inadequate basis for estimating cancer risks from long-term exposure to amitraz. The salient reasons for the Agency's decision not to grant conditional registration for the use of amitraz on apples are:

1) <u>The benefits of amitraz do not outweigh the potential risks for a 4 year period.</u> The potential benefits of the use of amitraz on apples are not significant. As stated in Position Document 3, the available alternative miticides are just as efficacious and cost less than amitraz. At most, amitraz might be used on 10% of the U.S. apple acreage. Amitraz could be used in rotation with other miticides to slow the development of mite resistance to these chemicals, but the "benefit" of this practice is speculative and not measurable. The insect suppression exhibited by amitraz is limited and would only be useful in certain pest complex situations. While amitraz appears to be less toxic to wildlife than the alternatives (except mineral oil), the actual hazards posed by amitraz and the alternatives to wildlife are not known. Oncogenic studies are not available for cyhexatin, but are available for propargite and mineral oil (Gregorio, 1979). Lifetime feeding of propargite to rats showed no oncogenic activity. The National Cancer Institute has established the non-carcinogenicity of mineral oil through its use of this compound as a vehicle for mixing and intubating animals in many bioassays.

On the risk side of the scale, the Agency has determined that there is weakly positive evidence to indicate amitraz is a potential human carcinogen. Accordingly,

applicators and persons eating treated fruit are believed to be exposed to a small cancer risk.

It is the Agency's conclusion that benefits would not exceed risks for a four year period of conditional registration, since the benefits of amitraz would be insignificant or speculative, some risk of cancer would be present, and efficacious and safe alternative miticides are available.

2) It is not in the public interest to approve the conditional registration of amitraz on apples. Section 3(c)(7)(C) of FIFRA requires the Administrator to determine that it is in the public interest to conditionally register a pesticide. This is a stringent test which requires that the benefits of the use of a particular pesticide must be very great in relation to any potential risks associated with that use. As indicated previously, the benefits of the use of amitraz on apples are limited and speculative. As for the risks, a small carcinogenic risk would exist for applicators and for humans consuming treated fruit. Therefore, the public interest test has not been met.

III. Conclusions

After reviewing the comments from the Secretary of Agriculture, the Scientific Advisory Panel and others concerning Amitraz Position Document 3, the Agency has confirmed its determination to conditionally register amitraz for pears and to not grant either full or conditional registration for use on apples.

The label for pears will be modified as follows:

1. Delete apron as a requirement during mixing and loading.

The conditional registration for pears is contingent upon the applicant for registration agreeing to submit:

1. A repeat mouse oncogenic bioassay conducted in accordance with protocols approved by the Agency.

2. Additional economic benefits data detailed in section II.C.1. of this document.

3. Annual reports of progress and available test results.

BIBLIOGRAPHY

Acme Reporting Company. (January 25, 1979). Transcript of Proceedings. Environmental Protection Agency. FIFRA Scientific Advisory Panel. Volume 1.

Albert, Roy E. (March 4, 1977) The Carcinogen Assessment Group's preliminary review of oncogenicity of Amitraz (BAAM). pp 22 (unpublished).

Albert, Roy E. (September 8, 1978a). Carcinogen Assessment Group's response to rebuttal comments for Amitraz. pp. 7.

Albert, Roy E. (September 5, 1978b). The Carcinogen Assessment Group's risk assessment on Amitraz (BAAM).

Albert, Roy E. (October 18, 1978c). Addendum to BAAM Rebuttal Analysis. pp. 5.

Albert, Roy E. (September 18, 1978d). CAG interim position regarding the carcinogenicity of BAAM. pp. 1.

Albert, Roy E. (December 21, 1978e). The Carcinogen Assessment Group's risk assessment on Amitraz.

Albert, Roy E. (March 2, 1979). Review of two additional pathogists' reports on BAAM. p.1.

Batchelor, G.S. and K.C. Walker, (1953). Health hazards involved in use of parathion in fruit orchards of north-central Washington. Ind. Hyg. & Occ. Med. pp. 522-529.

Beusch, G. (September 15, 1978). Graph of residue values (amitraz). Person communication to J. Kempter, Special Pesticide Review Division, OPP, EPA.

Budd, E.R. (June 30, 1978). Memo from Toxicity Branch Registration Division, EPA, concerning the dermal and lung penetration capability of amitraz (BAAM).

Burnett, R., J. Crowley, B. Lesse, D.S. G. Patton, M.M. Sutton, G.J.T. Turnbull, and G.A. H. Williams. (1976). BTS 27419: 80-week carcinogenicity study in mice-final report. The Upjohn Company, Kalamazoo, Michigan (unpublished). CONFIDENTIAL.

Bushong, C. (July 31, 1978). Revised fish and wildlife analysis. Ecological Effects Branch, Hazard Evaluation Division, EPA. pp. 100.

Clayson, D.B. (1975). Nutrition and experimental carcinogenesis: a review. Cancer Res. 35:3292-300 in UpJohn Rebuttal.

Cox, W.S., and Quick, R.S. (February 4, 1977). Memo from Chemists, Chemistry Branch, RD., OPP, and James Rea, Product Manager, Insecticide and Rodenticide Branch, RD, OPP, concerning analytical method and residue data for PP#6F1816 and FAP #6H5138 [amitraz in apples, pears, milk and meat].

Dale, L.B. (August 2, 1978). Toxicology Data on Alternative Pesticides to BAAM. Toxicology Branch, Hazard Evaluation Division, Office of Pesticide Programs, EPA. CONFIDENTIAL.

Davis, James E. (April 21, 1978 and May 15, 1978). Interim reports on the analysis of samples from environmental and occupational exposures to BAAM during the 1977 pear psylla program in the Wentachee area. EPA, Field Studies Section, Health Effects Research Laboratory, Wenatchee, Washington.

Dreer, R.A. (November 18, 1976) Memo from Acting Director, OSPR, OPP, to M.H. Rogoff, Associate Director for Scientific Review, RD, OPP, concerning RD referral of BAAM [amitraz] to OSPR for RPAR determination.

Entomological Society of America. (1977 and 1978). Insecticide and Acaricide Tests. Volumes 2, 3.

Environmental Protection Agency. (May 25, 1976). Interim Procedures and Guidelines for Health Risk and Economic Impact Assessment of Suspected Carcinogens. Federal Register, vol. 41:21401-21405.

Ford, J.H. (June 5, 1978). Collaborative study with Upjohn, SEA and APHIS on pear samples collected from the Northwestern United States. Memorandum to Dr. R.L. Williamson, Chief Staff Officer, Environmental Evaluation Staff, APHIS, USDA.

Garner, Willa. (1978a). Exposure analysis: Amitraz. Prepared by Chemist, Environmental Fate Branch, Hazard Evaluation Division, OPP, EPA.

Garner, Willa. (1978b). Addendum to 7/28/78 Exposure analysis for Amitraz. Environmental Fate Branch, Hazard Evaluation Division, OPP, EPA.

Garner, W. (1978c). Personal communication with Dr. James E. Davis, Field Studies Section, Environmental Protection Agency, Wenatchee, Washington. September, 1978.

Hutton, P.O. (1979). Memorandum to J. Kempter (SPRD/EPA) concerning review of benefits data for amitraz on apples.

Gregorio, C. (1979). Memorandum to J. Kempter (SPRD/EPA) concerning the oncogenic testing of alternatives to amitraz on apples.

Jegier, Z. (1964). Health hazards in insecticide spraying of crops. Arch. Environ. Health. 8:670.

Kakuk, T.J., [The Upjohn Company]. 1976. Viral induced lymphoreticular tumors in mice orally administered U-36059: supplemental report. 16 pp. (unpublished). CONFIDENTIAL.

Kuntz, B.T. (June, 1978). Economic implications of Amitraz (BAAM) use on pears. Agricultural Resources and Environmental Group, Natural Resource Economics Division, Economics, Statistics, and Cooperative Service, USDA. Corvallis, Washington.

Luttner, M. (June 27,1976). Memos from Economist, Economic Analysis Branch, BFSD, OPP, to Willa Garner, Chemist Environmental Fate Branch, HED, OPP, concerning number of applicators exposed to amitraz in pear and apple spraying operations.

Luttner, M. (March 2, 1977). Assessment of economic impacts resulting from non-availability of BAAM for pear psylla control in Oregon and Washington, 1977 crop year. Economic Analysis Branch, OPP, EPA. pp. 28.

McKissick, G.E. R.A. Griesemer, and R.L. Rarrell. (1970). Aerosol transmission of Rauscher murine leukemia virus. Jnl. Nat'l. Canc. Inst. 45:4(625-34) in Upjohn Rebuttal.

Roe, P.J.C. [The Boots Company,Ltd.] 1976. Opinion on the possible carcinogenicity of Amitraz (BTS 27419). 22 pp. plus Appendices. (unpublished). CONFIDENTIAL.

Rogoff, M.H. (October 15, 1976a). Memo from Associate Director for Scientific Review, RD, OPP, to R.H. Dreer, Acting Director, OSPR, OPP, referring BAAM [amitraz] to OSPR for RPAR review.

Turnbull, G.T. [The Boots Company, Ltd.] 1976. Revised notes on murine lymphosacroma. n.p. (unpublished). CONFIDENTIAL

Upjohn Company (EPA Co. No. 1023). 1976. Application for new pesticide product registration: BAAM (R) EC miticide/insecticide. Book VI, Upjohn discussion of toxicology section, Part 1. Kalamazoo, Michigan. (unpublished). CONFIDENTIAL.

Upjohn Company. (July 18, 1977). Rebuttal to the Rebuttable Presumption Against Registration and Continued Registration of Certain Products Containing Amitraz. Kalamazoo, Michigan. 4 volumes.

USDA/State Assessment Team on Amitraz. (August 11, 1978). Pesticide Impact Assessment: Amitraz [Benefits Analysis].

U.S. Environmental Protection Agency. (May 25, 1976). Health Risk and Economic Impact Assessments of Suspected Carcinogens. Federal Register, Vol. 41, pp. 21402-21405.

Vesselinovitch, S.D. 1976. Analysis of carcinogenicity bioassay data on Amitraz (BTS 27419, U-36059). n.p. (unpublished). CONFIDENTIAL

Weisburger, E.K. (May 8, 1978). Testing of 21 environmental aromatic amines or derivatives for long-term toxicity or carcinogenicity. Carcinogen Metabolism and Toxicology Branch, National Cancer Institute. unpublished.

APPENDIX A. LIST OF COMMENTS

[1(30000/2B)]: Michael Dover. January 16, 1979. Environmental Protection Agency. Memo to J. Kempter, EPA.

[2(30000/2B)]: Dr. Ross R. Herr. February 2, 1979. The Upjohn Company. Letter to EPA Federal Register Section.

[2A(30000/2B)]: Dr. Ross R. Herr. December 20, 1978. The Upjohn Company. Letter to Scientific Advisory Panel appending two proprietary pathologists' reports.

[2B(30000/2B)]: The Upjohn Company. December 20, 1978. Volume of benefits data submitted to J. Kempter, EPA.

[2C(30000/12B)]: Dr. Ross R. Herr. January 25, 1979. The Upjohn Company. Presentation to the Scientific Advisory Panel.

[2D(30000/12B)]: Dr. Thomas J. Kakuk, D.V.M. January 25, 1979. The Upjohn Company. Presentation to the Scientific Advisory Panel.

[3(30000/12B)]: Dr. H. Wade Fowler, Jr. February 2, 1979. Scientific Advisory Panel. Review of 6(b) action on amitraz (BAAM).

[4/30000/12B)]: Bob Bergland. February 14, 1979. U.S. Department of Agriculture. Letter to D. Costle, EPA.

[5/30000/12B]: Professor Angus J. Howitt. March 12, 1979. Cooperative Extension Service, East Lansing, MI. Letter to J. Kempter, EPA.

[6/30000/12B]: John R. Leeper and James P. Teete. March 19, 1979. New York State Agricultural Experiment Station. Letter to J. Kempter, EPA.

[7/30000/12B]: John Stover. April 2, 1979. Consulting Service, Pennville, Michigan. Letter to J. Kempter, EPA.

APPENDIX B. COMMENTS BY THE FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA) SCIENTIFIC ADVISORY PANEL

The Federal Insecticide, Funigicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel has completed review of plans by the Environmental Protection Agency (EPA) for initiation of regulatory action on amitraz pesticide products under the provisions of Section 6(b) of FIFRA as amended. The review was completed after an open meeting was conducted in Arlington, Virginia, during the period January 25-26, 1979.

Maximum public participation was encouraged during formal review of all aspects of the conclusion of the RPAR on amitraz. Federal Register notices announcing meetings in October, November, and January were published in the Federal Register on October 16, 1978, October 30, 1978, and January 18, 1979, respectively. The meeting announced in the Federal Register notice dated October 30, 1978, for November 15 and 16, 1978, was cancelled and rescheduled for January. In addition, telephone calls and special mailings were sent to the general public who had previously expressed an interest in activities of the Panel. Written statements relative to regulatory action on amitraz were received over

a period of several weeks from the Upjohn Company and Boots Ltd.; and expert witnesses which submitted documents in behalf of the Upjohn Company and Boots Ltd.; the Carcinogen Assessment Group of EPA; and EPA technical staff. In addition, oral comments were received from EPA staff; USDA staff; expert witnesses from New York State Agricultural Experiment Station; Cooperative Extension Service, University of California; Mid-Columbia Experiment Station, Oregon State University; members of the pesticide industry; and the general public.

In consideration of all matters brought out during Panel meetings, matters detailed in written and oral statements, and careful study of all documents submitted by the Agency, the Panel submits the following report on amitraz:

The trigger for the RPAR on BAAM is oncogenicity. The oncogenic potential of BAAM was raised initially by the pathologists of Boots Ltd. on the basis of a study in mice. The oncogenic potential of BAAM in this study was confirmed on reexamination of these data by Dr. Rueber, a consultant to EPA. A subsequent examination of these same data by Dr. Dubin, another consulting pathologist to EPA, failed to confirm a statistically significant increase in lymphoreticular tumors. However, in a reexamination of the data jointly by Dr. Dubin and Dr. Squire, another consulting

pathologist to EPA, indicated a statistically significant increase in lymphoreticular tumors in the BAAM exposed mice. Finally, a recent reexamination of the data by Dr. Lancaster, a pathologist for Boots Ltd. and Dr. Kakuk, a pathologist for the Upjohn Company, failed to reveal statistically significant differences in tumor incidence between BAAM exposed animals and untreated controls. From consideration of all these data, the Panel is of the opinion that a statistically significant increase in mouse lymphoma in BAAM treated mice has not been shown.

The FIFRA Scientific Advisory Panel agrees with the regulatory option under consideration by EPA for the use of BAAM on pears. This includes the use by certified applicators, an increased preharvest interval, the use of protective clothing, and reentry restrictions. As noted previously we are also recommending that a new mouse oncogenicity study be carried out.

The FIFRA Scientific Advisory Panel does not agree with the regulatory option choosen by the EPA for use of BAAM on apples. The Panel is of the opinion that the issue of oncogenicity of BAAM is sufficiently questionable that the restriction of the use of BAAM on apples is not warranted. The Panel is of the opinion that BAAM may prove to be of value in mite control on apples in some geographic areas of

the United States. The Panel also believes that the restriction of the experimental use of BAAM on other crops is not warranted from the current human risk data.

COMMENTS BY THE SECRETARY OF THE U.S. DEPARTMENT OF AGRICULTURE

This is the United States of Agriculture's response to the U.S. Environmental Protection Agency's (EPA) Notice of Determination pursuant to 40 CFR 162.11 (a)(5), concluding the Rebuttable Presumption Against Registration (RPAR) of Pesticide Products Containing Amitraz (BAAM).

The Department of Agriculture and State Cooperators, under the National Agricultural Pesticide Impact Assessment Program (NAPIAP), recognize the need to interact with EPA in developing biological, economic and exposure information according to the current Memorandum of Understanding between the Department and the Agency. We are also pleased to have the opportunity to review and comment on the Notice of Determination and the accompanying position document. We are dedicated to the mutual resolution of issues including health risks to applicators, farm workers, and consumers as well as possible adverse impacts on wildlife, non-target organisms and/or the environment.

We concur with EPA's selection or regulatory options that are consistent with the biological and economic assessments.

We, therefore, commend the decision that amitraz be retained for further evaluation under a "Conditional Registration" for four (4) years for use on pears with a one (1) day (24 hour) re-entry period and a seven (7) day preharvest interval.

The Department, however, believes the following concerns should be taken into consideration by the Agency in the development of the final regulatory decision:

I. We believe Experimental Use Permits for amitraz should be considered for use on apples. There are potential benefits for this use which should be explored. Permits should be granted to all states that express an interest and agree to demonstrate potential values with appropriate research and field evaluation. The reasons for this recommendation are:

   a. The two most widely used miticides for apples control only the mobile mite forms, while amitraz controls not only this form, but also the eggs and resting forms. Also, these materials are usually limited to postbloom and summer sprays. Amitraz has the versatility of being applied on a selective, as needed basis over the entire growing season, which permits use according to local conditions and circumstances.

b. It is true that amitraz is more costly to apply when compared to the other registered materials for mite control. However, amitraz also controls and/or suppresses other apple insect pests. When these "other" pests are a problem, additional insecticides must be applied for their control.

c. Amitraz may be a useful and needed tool in those areas where resistance to conventional miticides has been demonstrated.

d. Amitraz could be useful in apple growing areas as a late season "clean-up" spray to reduce overwintering populations.

It is probably true that amitraz will not perform significantly better than the registered apple miticides. However, when its relative safety, additional insects suppressed and/or controlled, usefulness in areas of resistance, and minimal hazard potential from ingestion of residues from treated fruit are considered, this action is warranted.

2. We have reservations on the practicality and enforceability of some of the Protective Clothing Regulatory Options under the General Precautions Section. Aprons are impractical and would cause a greater

risk of accidents when working around equipment. Considering the relative safety of amitraz, we do not understand the necessity for requiring both rubber gloves and the carrying of wash water and soap into the field for hand washing each time before eating, drinking, or smoking. We concur with the other General Precautions which provide adequate protection in this regard.

3. We do concur with the proposal to classify amitraz as a "Restricted Use Pesticide". The information presented to users in the certification training program for general and "Restricted Use" is that classification for "Restricted Use" really implies a definite concern over and above the precautions normally exercised in the handling, mixing, and application of pesticides. These precautions have been emphasized by registrants in labeling and in the education programs of Cooperative Extension for many years. All States have on-going educational programs and the people applying pesticides to commercial fruit trees are knowledgeable in the handling of pesticides. It is unreasonable to assume that when these applicators apply amitraz, they are going to relax, in any way, their application procedures. The highest exposure potential to

amitraz is during mixing loading, or application of the product. Again, the proposed precautionary labeling for protective clothing adequately covers this area.

We support the concept of "Restricted Use" and have devoted considerable time and funding to the development of State programs for certification. However, we believe that the "Restricted Use" classification should be limited to those pesticides that, when used as directed, pose a substantial risk to the user and/or the environment. We do not believe that amitraz falls into this category and strongly feel that a classification of "Restricted Use" may further dilute the sense of caution which should accompany "Restricted Use" pesticides.

World wide registrations have been obtained for amitraz not only on apples and pears but also on fruits, vegetables, hops, citrus, cotton, sheep, cattle and pigs. In the U.S., promising results have been obtained for mite control on citrus, strawberries, swine, dogs, and for the bollworm complex on cotton. American Agriculture should have the benefit of any effective pest control measures after they have been adequately researched and

registered. We feel that the Experimental Use Permits (EUP) and pending registrations for amitraz now held in abeyance by EPA because of the RPAR should be put back into the review process and evaluated on their own merits given the useful information and understanding that has resulted from this RPAR activity.

We are confident EPA will give favorable consideration to these suggestions and recommendations in developing the final amtiraz regulatory decisions. The opportunity to have cooperated on this important agricultural matter is very much appreciated by us as well as the whole agricultural community. Please let us know if additional information would be helpful.